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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,727	11/19/2001	Avi J. Ashkenazi	P27301C65	2390
35489	7590	08/10/2004	EXAMINER	
HELLER EHRMAN WHITE & MCAULIFFE LLP			ROMEO, DAVID S	
275 MIDDLEFIELD ROAD			ART UNIT	
MENLO PARK, CO 94025-3506			PAPER NUMBER	
			1647	

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/989,727

Applicant(s)

ASHKENAZI ET AL.

Examiner

David S Romeo

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 November 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 119-138 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 119-135 and 137 is/are rejected.
- 7) ☒ Claim(s) 136 and 138 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 0304, 0703, 1002
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

DETAILED ACTION

The preliminary amendments filed 09/03/2002 and 11/19/2001 have been entered.

Claims 119-138 are pending and being examined.

5

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

10

Priority

According to the communication of 09/03/2002, the present application is claiming priority under 35 U.S.C. 120 and 119 (e) to earlier filed applications. Under 35 U.S.C. 120, the claims in a U.S. application are entitled to the benefit of the filing date of an earlier filed U.S. application if the subject matter of the claim is disclosed in the manner provided by 35 U.S.C. 112, first paragraph in the earlier filed application. Under 35 U.S.C. 119 (a) or (e), the claims in a U.S. application are entitled to the benefit of a foreign priority date or the filing date of a provisional application if the corresponding foreign application or provisional application supports the claims in the manner required by 35 U.S.C. 112, first paragraph. A deficiency under 35 U.S.C. 101 also creates a deficiency under 35 U.S.C. 112, first paragraph.

The earliest filed prior application that establishes a utility for the presently claimed PRO1186 polynucleotide and, hence, provides a disclosure in the manner provided by 35 U.S.C. 112, first paragraph, is U. S. Application No. 60/145,698 (filed

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07/26/1999), which discloses the ability of the PRO1186 polypeptide to stimulate adrenal cortical capillary endothelial cell (ACE) growth. Accordingly, the effective filing date of the presently claimed compounds is 07/26/1999.

Should Applicants disagree with the examiner's determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent application filed prior to 07/26/1999 which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of and fully enabled for prior to 07/26/1999.

According the preliminary amendment filed 09/03/2002 this application is a CON of 09/941,992, filed 08/28/2001, which claims the benefit of 60/213,637, filed 06/23/2000, and 60/230,978, filed 09/07/2000. The benefit claim to 60/213,637, filed 06/23/2000, is not proper because it must be filed within twelve months from the filing date of the provisional application. Any nonprovisional application that directly claims the benefit of a provisional application under 35 U.S.C. § 119(e) must be filed within twelve months from the filing date of the provisional application. If a benefit claim to a provisional application is submitted without an indication that an intermediate nonprovisional application directly claims the benefit of the provisional application and the instant nonprovisional application is not filed within the twelve month period, the Office will not have sufficient information to enter the benefit claim into the computer database. Therefore, the Office will not recognize such a benefit claim.

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Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(f) he did not himself invent the subject matter sought to be patented.

Claims 119, 120, 132-135, 137 are rejected under 35 U.S.C. 102(a or b) as being anticipated by Strausberg.

This rejection is being made under 35 U.S.C. § 102(a) in the event that applicant shows that they are entitled to the benefit of a priority date that is after March 27, 1998 and on or before March 27, 1999.

This rejection is being made under 35 U.S.C. § 102(b) in the event that applicants are unable to show that they are entitled to the benefit of a priority date that is on or before March 27, 1999.

Strausberg discloses an isolated nucleic acid molecule that has a Best Local Similarity of 96.4% over almost its entire length to SEQ ID NO: 370, as indicated below (Db = Strausberg's nucleic acid molecule):

Query Match 26.7%; Score 377.6; DB 9; Length 423;
Best Local Similarity 96.4%; Pred. No. 8.8e-92;
Matches 397; Conservative 0; Mismatches 14; Indels 1; Gaps 1;

Qy	148	GCTGTGATCACAGGGGCCTGTGAGCGGGATGTCCAGTGTGGGGCAGGCACCTGCTGTGCC	207
Db	423	GCTGTGATCACAGGGGCCTGTGAGCGGGATGTCCAGTGTGGGGCAAGACACTGCTGTGCC	364
Qy	208	ATCAGCCTGTGGCTTCGAGGGCTGCGGATGTGCACCCCGCTGGGGCGGGAAGGCGAGGAG	267
Db	363	AATCACCTGTGGCTTCGAGGGCTGCGGATGTG-ACAAACCTGGGGCGGGAAGGCGAGGAG	305
Qy	268	TGCCACCCCGGCAGCCACAAGGTCCCTTCTTCAGGAAACGCAAGCACCCACACCTGTTCCT	327

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5 Db 304 TGCCACCCCGGCAGCCACAAGGTCCCCCTTCTTCAGGAAACGCAAGCACCACACCTGTCCT 245

Qy 328 TGCTTGCCCAACCTGCTGTGCTCCAGGTTCCCGGACGGCAGGTACCGCTGCTCCATGGAC 387

5 Db 244 TGCTTGCCCAACCTGCTGTGCTCCAGGTTCCCGGACGGCAGGTACCGCTGCTCCATGGAC 185

Qy 388 TTGAAGAACATCAATTTTTAGGCGCTTGCTGGTCTCAGGATACCCACCATCCTTTTCCT 447

10 Db 184 TTGAAGAACATCAATTTTTAGGCGCTTGCTGGTCTCAGGATACCCACCATCCTTTTCCT 125

Qy 448 GAGCACAGCCTGGATTTTTATTTCTGCCATGAAACCCAGCTCCCATGACTCTCCAGTCC 507

Db 124 GAGCACAGCCTGGATTTTTATTTCTGCCATGAAACCCAGCTCCCATGACTCTCCAGTCC 65

15 Qy 508 CTACACTGACTACCTGATCTCTTGTCTAGTACGCACATATGCACACAGG 559

Db 64 CTACACTGACTACCTGATCTCTTGTCTAGTACGCACATATGCACACAGG 13.

Strausberg's nucleic acid molecule would meet all the limitations of claims 132-

134, in the absence of evidence to the contrary.

20 Strausberg's nucleic acid molecule is at least 87% identical to nucleotides 148-405 of SEQ ID NO: 370, i.e., "a nucleic acid sequence encoding the polypeptide shown in Figure 266 ..., lacking its associated signal peptide," as indicated below (Db = Strausberg's nucleic acid molecule)

25 Query Match 87.3%; Score 227.8; DB 9; Length 423;
Best Local Similarity 95.0%; Pred. No. 5.8e-42;
Matches 246; Conservative 0; Mismatches 12; Indels 1; Gaps 1;

30 Qy 1 GCTGTGATCACAGGGGCCCTGTGAGCGGGATGTCCAGTGTGGGGCAGGCACCTGCTGTGCC 60

Db 423 GCTGTGATCACAGGGGCCCTGTGAGCGGGATGTCCAGTGTGGGGCAAGACACTGCTGTGCC 364

Qy 61 ATCAGCCTGTGGCTTCGAGGGCTGCGGATGTGCACCCCGCTGGGGCGGGAAGGCGAGGAG 120

35 Db 363 AATCACCTGTGGCTTCGAGGGCTGCGGATGTG-ACAAACCTGGGGCGGGAAGGCGAGGAG 305

Qy 121 TGCCACCCCGGCAGCCACAAGGTCCCCCTTCTTCAGGAAACGCAAGCACCACACCTGTCCT 180

Db 304 TGCCACCCCGGCAGCCACAAGGTCCCCCTTCTTCAGGAAACGCAAGCACCACACCTGTCCT 245

40 Qy 181 TGCTTGCCCAACCTGCTGTGCTCCAGGTTCCCGGACGGCAGGTACCGCTGCTCCATGGAC 240

Db 244 TGCTTGCCCAACCTGCTGTGCTCCAGGTTCCCGGACGGCAGGTACCGCTGCTCCATGGAC 185

45 Qy 241 TTGAAGAACATCAATTTTT 259

Db 184 TTGAAGAACATCAATTTTT 166.

Claims 199-135, 137 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Applicants purchased a clone containing the

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cDNA insert shown in FIG. 265 (SEQ ID NO: 370). See page 497 of the present application.

Claim Rejections - 35 USC § 112

5 The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10 The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15 Claims 119-123, 132-138 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding a polypeptide having at least 80% identity to a polypeptide comprising the amino acid sequence of SEQ ID NO: 371 or a polypeptide comprising the amino acid sequence of SEQ ID NO: 371 lacking its associated signal peptide, wherein the claimed
20 polynucleotide encodes a polypeptide that is limited by a functional activity that is specific and substantial for a polypeptide comprising the amino acid sequence of SEQ ID NO: 371, does not reasonably provide enablement for a polynucleotide encoding polypeptide that is not identical to at least a polypeptide comprising the amino acid sequence of SEQ ID NO: 371 lacking its associated signal peptide without regard to the
25 functional activity of the encoded polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

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The claims are drawn to polynucleotides encoding polypeptides having at least 80% amino acid sequence identity to the polypeptide of SEQ ID NO: 371, to said polypeptide lacking its associated signal peptide, or to the extracellular domain thereof. The claims are also drawn to hybridizing polynucleotides. There is no functional

5 limitation in the claims.

The claim encompasses an unreasonable number of polynucleotides encoding inoperative polypeptides, which the skilled artisan would not know how to use. While the specification suggests that the polypeptide of SEQ ID NO: 371 is a secreted polypeptide, secreted polypeptides have widely varying activities. See page 1, lines 8-15.

10 Therefore, knowledge that a protein is secreted does not provide predictability regarding. Furthermore, mere hybridization is not a substitute for producing a functional protein because of the number of nucleotide substitutions, insertions, and deletions encompassed by the hybridization language that encode a corresponding number of amino acid substitutions, insertions, deletions, and truncations.

15 There are no working examples of polynucleotides encoding polypeptides less than 100% identical to the SEQ ID NO: 371. The skilled artisan would not know how to use polynucleotides encoding non-identical polypeptides on the basis of teachings in the prior art or specification unless they encoded polypeptides that functioned in a manner consistent with the function the PRO1186 polypeptide. The specification does not

20 provide guidance for using polynucleotides encoding polypeptides related to (i.e., 80%-99% identity) but not identical to the PRO1186 polypeptide. The claims are broad because they do not require the claimed polynucleotides to be identical to the disclosed sequence and because the claims have no functional limitation.

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For these reasons, which include the complexity and unpredictability of the nature of the invention and art in terms of the diversity of secreted proteins and lack of knowledge about function(s) of encompassed polypeptides structurally related to PRO1186, the one limited working examples of PRO1186 polypeptide and its function, the lack of direction or guidance for using polynucleotides encoding polypeptides that are not identical to PRO1186, and the breadth of the claims for structure without function, it would require undue experimentation to use the invention commensurate in scope with the claims.

Claims 119-123, 132-138 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polynucleotides encoding polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence or to polynucleotides that hybridize to polynucleotides encoding SEQ ID NO: 371. The claims do not require that the polynucleotides possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polynucleotides that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial

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structure, physical and/or chemical properties, functional characteristics,
structure/function correlation, methods of making the claimed product, or any
combination thereof. In this case, the only factor present in the claim is a partial structure
in the form of a recitation of percent identity or hybridization. There is not even
5 identification of any particular portion of the structure that must be conserved.

Accordingly, in the absence of sufficient recitation of distinguishing identifying
characteristics, the specification does not provide adequate written description of the
claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states “applicant must
10 convey with reasonable clarity to those skilled in the art that, as of the filing date sought,
he or she was in possession of the invention. The invention is, for purposes of the
'written description' inquiry, whatever is now claimed.” (See page 1117.) The
specification does not “clearly allow persons of ordinary skill in the art to recognize that
[he or she] invented what is claimed.” (See Vas-Cath at page 1116). As discussed above,
15 the skilled artisan cannot envision the detailed chemical structure of the encompassed
genus of polynucleotides, and therefore conception is not achieved until reduction to
practice has occurred, regardless of the complexity or simplicity of the method of
isolation. Adequate written description requires more than a mere statement that it is part
of the invention and reference to a potential method of isolating it. The compound itself
20 is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc.
v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30
USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be

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unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polynucleotides encoding polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 337, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 119-124, 127, 128, 132-138 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The PRO1186 polypeptide is disclosed as a soluble or secreted protein, and is not disclosed as being expressed on a cell surface. Accordingly, the limitation “extracellular domain” is indefinite, as the art does not recognize soluble or secreted proteins as having such domains. Further, if the protein had an extracellular domain, the recitation of “the extracellular domain ... lacking its associated signal sequence” is indefinite as a signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell. The metes and bounds are not clearly set forth.

Claim 133 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 133 is indefinite over the recitation of “stringent

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conditions” because stringency varies according to the hybridization conditions and the particular hybrid under study. The specification fails to limit the definition of “stringent conditions.” The metes and bounds are not clearly set forth.

Conclusion

Claims 136, 138 are objected to as being dependent upon a rejected base claim.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571) 272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHT FAX NUMBERS:

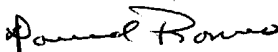
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FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0890.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.



DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
AUGUST 3, 2004